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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,392	11/23/2001	George Jackowski	2132.097	4945

21917 7590 04/23/2003

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1641	7

DATE MAILED: 04/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,392	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) 3-9, 29-38 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,2 and 10-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-2 and 10-28, drawn to biopolymer markers, classified in class 436, subclass 512.

   II. Claims 3-9, drawn to a method for evidencing and categorizing at least one disease state, classified in class 435, subclass 69.2.

   III. Claims 29-32, drawn to a diagnostic assay kit for determining the presence of the biopolymer markers or analytes, classified in class 436, subclass 86.

   IV. Claims 33-38, drawn to a process for identifying therapeutic avenues related to a disease, classified in class 422, subclass 119.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and (II, IV) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the products from invention I, can be practiced with another materially different process other than inventions II and IV, such as isolation and separation of the specific analytes.

3. Similarly, inventions III and (II, IV) are also related as product and process of use. Likewise, invention III can be practiced by materially different process other than inventions II and IV, such as isolation and separation.

4. Inventions I and III are patentably distinct and unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case invention I is directed to biompolymers consisting of specific polypeptides, whereas invention III is directed to polyclonal antibodies produced against the polypeptide

markers. Both polypeptides and antibodies are patentably distinct in terms of structure and functions. Therefore, inventions I and III are distinct and unrelated inventions.

5. Inventions II and IV are patentably distinct and unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case invention II and IV are distinct and unrelated inventions. The feature of conducting mass spectrometric analysis and correlation of isolated biopolymer markers with normal and patients in invention II, is not required by the claims of invention IV. The feature of using biopolmer markers and its variants or moieties as direct therapeutic modalities, either alone or in conjunction with an effective amount of a pharmaceutically effective carrier in invention IV, is not required by the claims of invention II.

6. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, and the search required for one group is not required for the other, therefore restriction for examination purposes as indicated is proper.

7. During a telephone conversation with Mr. Landers on January 15, 2003, a provisional election was made without traverse to prosecute the invention of group I, claim1-2, 10-28. Affirmation of this election must be made by applicant in replying to this Office action. Claim3-9, 29-32 and 33-38 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

Enablement

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 10-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The invention is directed to identify a particular disease, i.e. insulin resistance, by determining the presence of certain biomarkers in the sample, such as SEQ ID NO. 1, 2 or 3. However, the prior art of record fails to disclose a method for *predicating* insulin resistance disease state. There is lack of sufficient support in the specification shows that the instant recited SEQ ID No. 1-3 can be unequivocally served as the biomarkers for insulin resistance disease. Applicants assert that Figure 1, *"a photograph of a gel which is indicative of the presence/absence of the marker in disease vs. control, ..."* (page 46, third paragraph) Applicants further assert that different bands, i.e. proteins now designated as SEQ ID No. 1, 2 or 3 in the instant application, *"related to Insulin Resistance were found."* (supra, second paragraph) and the relative strength, e.g. the up or down regulation of the marker relative to categorization of disease state is deduced. (supra, third paragraph)

(1) However, there are still several fatal defects that fail to enable the instant invention. First, it is not clear how many patient samples were used in this experiment. In another word, applicants lack of statistical evidence, e.g. sufficient sample size and statistical coefficient parameter, necessary for claiming the proteins appear on the gel correlate to the occurrence or development of insulin resistance disease. Second, it is not clear how Figure 1 was conducted, particularly what source of samples applicants used. Are the sample source collected from

(2)

blood, saliva, or urine? Third, no evidence supports the notion that appearing a different protein certainly attributes to the occurrence of a particular disease. There remains various uncertain "missing boxes", e.g. different physiological or pathological developments, from protein synthesis down to the phenotype of the specified disease. Fourth, it is not clear what bands appeared on the gel of Figure 1 corresponding to SEQ ID No. 1, 2 or 3. Or what band(s), i.e. proteins, is down or upregulated corresponding to the occurrence of the asserted insulin resistance. Fifth, Figure 1 shows the occurrence of various proteins of the insulin resistance v. normal. To be a specific biomarker for a particular disease, the marker must be sufficiently specific to distinguish one disease from the other in order to avoid false positive results. As indicated by applicant, high blood pressure and obesity could also result in insulin resistance (page 30, line 15-18). Therefore the instant invention lacks specificity to differentiate the insulin-related resistance diseases. Taken together, the relative of skill in the field is high, and it would require undue amount of experimentation for the skilled artisan to confirm the recited biopolymers can be served as biomarkers in diagnosis of diseases.

Utility

10. Claims 1-2 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility.

The asserted utility of the biomarkers of claim 1-2 is for indicating at least one particular disease state, i.e. use in a diagnostic method. However, applicant fails to present concrete and convincing evidence recognized in the art in support of the asserted diagnostic method by using the recited amino acid biomarkers. (See discussion *supra*) Furthermore, prior arts have identified SEQ ID No. 1 and 2 as indicators of fatty acid metabolism and psychological disorder, respectively, *other than* the asserted indicative of insulin resistance disease. (See Rejection under 35 U.S.C. 102 below)

Specifically, since the claimed biomarkers are not supported by either a specific and credible asserted utility or a well established utility for the reasons set forth above, one skilled in

the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. Supra.

35 U.S.C. § 112, Second Paragraph

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-2, 10-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 1, "at least one analyte thereof," is vague and confusing. It is unclear how a material can be an analyte of a biopolmer marker.

Similarly, claims 10, 18 and 28 share the same problem as claim 1.

With respect to claim 1, "indicating at least one particular disease state" is vague and indefinite. It is unclear what specific disease(s) applicant refers to.

With respect to claim 2, line 1" if insulin" should be -- of insulin--.

With respect to claim 12, "at least one labeled biochemical material," vague and indefinite in relation to claim 10 from which it depends in reciting, "at least one labeled biochemical material" because it is unclear as to whether the biochemical material in the instant claim is the same as the biochemical material recited in claim 10, but including a label. Perhaps, Applicant intends the labeled biochemical material to be a second biochemical material that is conjugated to a label.

Similarly, claim 14 shares the same problem as claim 12.

Claim 17, "therefore" should be "thereof."

Claim 25 shares the same problem as claim 17.

With respect to claims 23 and 24, "the sample" lack antecedent basis.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 are rejected under 35 U.S.C. 102 (b) as being anticipated by Borden et al. (WO9604790)

Borden et al. teach using various mammalian betaine-gamma-aminobutyric acid transporter comprising the recited SEQ ID No. 2 (See SEQ No. 1, residue 583-595) Borden et al. also teach using the markers for screening and diagnosis of GABA associated abnormalities,

particularly psychiatric disorder. (Abstract) The reason for rejection claim 2 is on the ground that the intended use in claim 2 is not given any patentable weight because of the nature of the product claim. Therefore, claim 2 is also anticipated by Borden et al..

Claims 1-2 are rejected under 35 U.S.C. 102 (b) as being anticipated by Waterham et al. (Biochem. Biophys. Res. Commu. (1999) 263: 213-218)

Waterham et al. teach cloning human carnitine octanolyltransferase comprising the recited SEQ ID No. 1 (See residue from 187-198). Similarly, claim 2 is rejected on the ground of its dependence on the parent claim. See supra.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. Claims 1-2, 10-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borden et al. in view of Hutchens et al. (USP 6225047).

Borden et al reference has been discussed but does not teach a kit for detecting the biopolymer markers of Borden et al. Hutchens et al. disclose a method and kit for identifying biopolymer markers (diagnostic markers) representative of or capable of categorizing specific disease states using Surface Enhanced Laser Desorption Ionization Spectrometry Mass Spectrometry (SELDI-MS). Hutchens et al. specifically disclose obtaining a sample, exposing the sample to a substrate for use in SELDI-MS that comprises at least one addressable location, each addressable location comprising an adsorbent species such as antibody immoblilized into the substrate on a solid support, that resolves at least one of the biopolymers under elution conditions, and then subjecting the sample to SELDI-MS. (Figure 1 and 2) The adsorbent species may also be a biochemical material (metal chelator or anion exchange material) (see column 5, lines 41-43, column 7, lines 11-41, and column 13, lines 47-58). The sample may be unfractionated body fluid such as blood, urine, blood products, i.e. serum, or tissue sample. The method and kit may be applied to multiple samples (see column 8, lines 45-53). Hutchens also teach using antibody adsorbed on the substrate to detect specific analyte. (Col. 4, line 25-29 and Figure 14) The antibody is monoclonal and labeled with a detectable moiety which generates a measurable signal such as radioactive, chromogenic, or fluorescent (see column 15,m line 59 to column 16, line 25). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teaching of Borden et al. of SEQ ID NO. 2 which comprises a biopolymer used as a diagnostic marker of a disease state, i.e. insulin resistance (*argumentatively in this case)*, with the method of Hutchens which uses SELDI-MS for differential detection of biopolymers by antibody binding to the specific analyte because the teachings of Hutchens specifically taught to resolve different biomarkers for clinical diagnosis purposes. (Col. 7, line 32-40)

Conclusion

18. `No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 703-306-4086. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-305-3399.

Jacob Cheu
Examiner
Art Unit 1641

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
4/21/03

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April 21, 2003